Appl. No.: 10/076,727
Amdt. Dated: 02/03/2006
Off. Act. Dated: 08/03/2005

REMARKS/ARGUMENTS

By the Office Action mailed on August 3, 2005, claims 7-20 are pending and under examination. Applicants mailed a response to the Office action to provoke an advisory action on October 3, 2005. The Office mailed an Advisory Action on October 28, 2005. which stated that the amendments to the claims were not allowed and arguments presented were predicated on the proposed claim amendments which were not entered. Claims 7-20 were rejected. Claims 7. 8. 9, 14, and 17 are currently amended. Claims 25 and 26 are newly added and find support at pages 5-7 of the specification. Claims 1-6. and 21-24 are cancelled. These claims have been cancelled not in acquiescence to any rejection, but solely in the interest of Applicants' patent and business goals.

Applicants submit that the amendments to the claims do not incorporate new matter. Claims 7, 8, 9. 14, and 17 have been amended to better describe the doped lipid bilayer nature of membranes used in the claimed methods and to further Applicants' patent and business goals. Support for these amendments can be found in the specification at pages 4-10 and 12. For example, at the last sentence of the Abstract, paragraph [0088], it states: "The lipid bilayer membranes are doped with various lipids and/or proteins to modulate the adherence of the cells being used in the device."

For the sake of clarity, the rejections and objections of the presently outstanding Office Action are set forth below, in the order in which they were presented and are herein addressed:

1. Claims 7-20 stand "rejected under 35 U.S.C. 102(e) as being anticipated by Kam et al., U.S. publication number 2002/0009807.
2. Claims 7. 8, 14, 15, and 16 stand "rejected under 35 U.S.C. 102(e) as being anticipated by Chen et al. U.S. publication number 2002/0182633."
3. Claims 7-20 stand "rejected under 35 U.S.C. 103(a) as being obvious over Chen et al., U.S. Publication number 2002/0182633 and Boxer et al., U.S. Patent number 6,228,326.

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I. Rejection of Claims 7-20 under 35 U.S.C. § 102(e)

Claims 7-20 have been rejected under 35 U.S.C. 102(e) as being anticipated by Kam et al., U.S. publication number 2002/0009807. Applicant respectfully traverses these rejections as argued below, and requests reconsideration.

For a claim to be rejected under 35 U.S.C. 102(e) as being anticipated, each element and limitation must be taught. Referring now to amended claim 7, Applicants assert that Kam fails to teach each and every claimed limitation of claim 7 of observing cell adhesion to the doped lipid bilayer membranes, the limitations on the micro-array device requiring an aqueous layer between the substrate and the lipid bilayer, that the lipid bilayer membranes are doped with "dopants selected from the group consisting of charged lipids, membrane proteins, and signaling proteins; and finally that observing cell interaction and adhesion to the doped lipid bilayer membranes occurs "after a time period of at least one hour, whereby the dopants direct cell adhesion, and wherein the cell interaction is a functional and natural interaction."

Furthermore, Kam discloses the use of fibronectin as a barrier material and cell adhesion compatible material, and does not disclose the use of lipids to direct cell adhesion. In fact, Kam teaches that the "cells adhere only to the cell adhesion compatible material and not to the lipid bilayer expanse." See Kam et al at column 2, paragraph [0031]. Applicants respectfully point the Examiner to Figure 1A of Kam et al. which shows that in the arrays of Kam, cells only adhere to the cell adhesion compatible material (i.e., fibronectin) used to construct the device. Thus, Kam only teaches cell adhesion to fibronectin barriers deposited directly on the substrate, and not to the lipid bilayer expanse interspersed between such barriers.

Therefore, Kam does not anticipate Applicants' claim 7 as amended, and in fact teaches away from Applicants' invention in that Kam teaches the cell adhesion compatible material is also the static barrier material, not the fluid lipid bilayer as taught by Applicants' claimed invention. Kam teaches instead "cells adhere only to said cell adhesion compatible material and not to said lipid bilayer expanse" (Kam claim 2, last three lines).

The Office Action states on page 5 that "[i]n a method for screening for a result,...observance of a negative result still falls within the metes and bounds of the claimed method." While a negative result may fall within the metes and bounds of the claimed invention, however, Claim 7 is a method for screening living cell adhesion with the limitation of observing

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cell interaction and adhesion *whereby the dopants direct cell adhesion*. Applicants submit that Kam does not teach or suggest this claimed limitation. Therefore, because Kam does not anticipate and teaches away from the claimed invention, the rejection of claim 7 should be properly withdrawn.

Applicants assert the Kam does not anticipate claim 8 because Kam fails to teach the following limitations of claim 8 of "determining the adhesion of the cells to the lipid bilayer membranes in different corrals by observing cell adhesion to said lipid bilayer membranes having different compositions," and the limitation that the dopants to direct cell adhesion are selected from the group consisting of charged lipids, membrane proteins, and signalling proteins. As argued above, Kam teaches directly away from such adhesion by instead teaching cell adhesion only to the "bilayer barrier regions further comprised of a cell adhesion compatible material," *e.g.* fibronectin (Kam, claim 1, line 8). Therefore, because Kam et al. does not teach each and every limitation of the claimed invention, Applicants submit that claim 8 is not anticipated and respectfully request that the rejection of claim 8 be withdrawn.

Applicants also request that the rejection as to anticipation of claims 9-13 be withdrawn as they depend from claim 8, which as argued above is not anticipated by Kam.

Applicants' Claim 14 similarly contains the limitation of "observing cell adhesion to the lipid bilayer membranes". For the same reasons as previously recited above, Kam fails to teach cell adhesion to membranes. Therefore, for the same reasons as above, Applicants respectfully traverse the rejection and kindly request reconsideration of this claim.

Because dependent claims 15-20 incorporate all of the limitations of base claim 14, and for the same reasons given above should also not be taught by Kam. Therefore, Applicants respectfully assert that Kam does not anticipate claims 7-20 and request that these rejections be withdrawn.

II. Rejection of Claims 7, 8, 14, 15 and 16 under 35 U.S.C. § 102(e)

Claims 7, 8, 14, 15, and 16 stand "rejected under 35 U.S.C. 102(e) as being anticipated by Chen et al. U.S. publication number 2002/0182633."

Applicants submit that Chen et al. does not anticipate Applicants' claimed invention because Chen does not teach each and every limitation as claimed. Chen does not teach methods

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for observing and determining cell adhesion of living cells having the limitations of Applicants' invention. Chen describes the use of adhesive species such as ECM, *i.e.*, extracellular matrix proteins such as fibronectin, and non-adhesive species, *i.e.*, PEO lipids, to enable patterning and customized cell environments. See paragraph [0102] of Chen, recited in the Office action on page 7. Applicants' claims recite methods using micro-arrays having lipid bilayer membranes that are doped with dopants selected from charged lipids, membrane proteins, and signaling proteins, whereby the dopants direct cell adhesion.

Applicants disagree that one having skill in the art would read Chen as contemplating the use of PEO lipids in lipid bilayer membranes for cell adhesion. Applicants address the Office's characterization of the use of PEO in Chen et al. In Chen, PEO is consistently used as a surfactant for the express purpose of specifying non-adhesive domains. See the following paragraphs in Chen et al: 59, 101, 102, 103, 120, 129, 132, and 134. The single recitation of "PEO lipid bilayers" in paragraph [0102] was in reference to the possible use of specially modified poly(ethylene oxide) lipid bilayers to micropattern non-adhesive domains. The Examiner cited the specific paragraph on page 7 of the Office Action only to ignore the fact that Chen et al. recite that PEO is a "non-adhesive (PEO) species." (Chen, Column 10, line 5). Thus, Chen contemplates the use of PEO lipids as taught by Dori et al, **for the sole purpose of patterning non-adhesive domains.**

Therefore, because Chen does not teach the use of doped lipid bilayers for modulated selective cell adhesion, nor does Chen teach the dopants claimed, the reference cannot be seen as anticipating Applicant's claimed invention. For a reference to be a proper 35 U.S.C. 102(e) reference, it must teach all elements and limitations of a claimed invention. Applicants assert that Chen et al. fails in this regard and Applicants respectfully request that the rejection be withdrawn.

III. Rejection of Claims 7-20 under 35 U.S.C. § 103(a)

Claims 7-20 stand "rejected under 35 U.S.C. 103(a) as being obvious over Chen et al., U.S. Publication number 2002/0182633 and Boxer et al., U.S. Patent number 6,228,326."

MPEP § 2143 requires that "[t]o establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references

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themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

"To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, to modify the reference or to combine reference teachings as discussed in subsection 3 (b) MPEP 2143.03. Additionally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985) MPEP 2142.

The independent claims 7, 8, and 14 have been amended to include the limitations that the fluid lipid bilayer membranes are doped with dopants selected from the group of charged lipids, membrane proteins, and signaling proteins. Furthermore, the claims recite the limitation that the dopants direct adhesion and the resulting interaction is a natural and functional interaction. It is submitted that these claim limitations appear in none of the cited 35 USC 103(a) references.

Applicants submit it would not have been obvious to use the methods described by Chen combined with Boxer's biosensor because Chen's methods are directed to using static or immobilized proteins such as fibronectin and other ECM proteins to pattern cell adhesion. Combining Chen's methods with Boxer's biosensor would not produce the claimed methods, but instead would teach methods of using the microcontact printing system of Chen, ECM proteins to promote adhesion, with Boxer's supported membrane biosensor device. It could be argued that the resulting device would be similar to the device described by Kam et al., US 2002/0009807, cited above, to which Applicants have argued does not anticipate or suggest Applicants' claimed invention.

In contrast, the claimed invention relies on dopants in the lipid bilayer to direct cell adhesion (e.g., charged lipids, membrane proteins, signaling proteins), which are fluid and mobile, not immobilized proteins such as fibronectin. In Applicants' invention, the cells adhere

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to dopants *in the lipid bilayer*, thereby allowing cells to establish and maintain functional and natural interaction with the lipid bilayer. Furthermore, the dynamic lipid bilayer membranes closely model segments of intact cell walls, and thus the claimed methods are useful for observing and establishing cell-cell interaction studies. In contrast, the combination of Chen and Boxer would result in methods and a device useful for studying cell-ECM interactions. The cell-cell interactions that are generated by the present claimed methods are altogether different than the cell-ECM interactions generated by the combination of the cited references, Chen et al. and Boxer et al. Applicants have attached a review article (Exhibit A) written by the first named inventor, John (Jay) T. Groves, entitled "Learning the Chemical Language of Cell-Surface Interactions," *Sci STKE*. 2005 Sep 13;2005(301):pe45, which describes the differences between the two types of interactions.

Thus, Applicants assert that one having skill in the art would not seek to combine the two references for the purpose of practicing Applicant's claimed methods because the practice of Chen methods with Boxer's biosensor device will necessarily employ the use of ECM proteins for cell adhesion and not the methods of doping taught by Applicants to direct cell adhesion to lipid bilayer membranes. Therefore Applicants assert that since neither reference teaches or suggests the methods of Applicants' claimed invention, it would not have been obvious to combine Chen and Boxer to result in Applicants' claimed methods.

Applicants submit the Examiner has failed to establish a *prima facie* case of obviousness as set forth above for the various 35 U.S.C. 103(a) rejections addressed above. Applicants respectfully request that the rejection be withdrawn and the claims allowed.

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CONCLUSION

Applicants respectfully urge the Examiner to withdraw all rejections in view of the foregoing arguments presented. For the reasons set forth above, Applicants respectfully request that the accompanying amendments to the claims be entered and considered for this case.

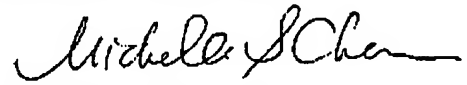
Applicants hereby request a Three-Month Extension of time from November 3, 2005 to February 3, 2006. Please charge the fee of $510.00 according to the petition for an extension of time included herewith in duplicate.

Please charge a fee of $395.00 for the Request for Continued Examination according to the Fee Transmittal included herewith in duplicate. The Director is authorized to charge fees of $905.00 total in accordance with the enclosed fee calculation sheets for the Request for Continued Examination and the extension of time. Please charge any necessary and additional fees or make any credits that may be due to Deposit Account No. 120690.

Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned at (510) 495-2456.

Date: February 3, 2006

Respectfully submitted,



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